REMARKS

Reconsideration of the present application is requested in view of the foregoing amendments and following remarks, which are believed to address all outstanding issues in the application and simplify issues for Allowance or Appeal.

I. Claim Amendments

Claim 1 is amended to insert a comma.

Claim 4 is amended to clarify the nature of the substrate binding site.

Claim 33 is amended to correct its dependency.

Claim 9 is canceled without prejudice or disclaimer.

No new matter is added by these amendments.

II. Claim Objections

Claim 33 was objected to for depending from itself.

Claim 33 has been ameded to depend from claim 32 to address the objection.

III. Rejections under 35 U.S.C. §112, second paragraph

Claims 1-5, 7-9, 19-23, 25, 26, and 32-36 were rejected under 35 U.S.C. §112, second paragraph, as allegedly being indefinite with respect to whether the antagonist comprsises the targeting moiety and the enzyme. The rejection is traversed.

Claim 1, as amended to correct punctuation, and from which all other claims depend, is drawn to "[a] catalytic antagonist of a target molecule, said antagonist comprising *a targeting moiety* that specifically binds to said target molecule, said *targeting moiety being a carbohydrate attached to an enzyme*, said enzyme being a subtilisin-type serine protease that degrades said target molecule to reduce binding of the target molecule to its cognate ligand and to said targeting moiety thereby resulting in the release of said antagonist thereby allowing said antagonist to bind and degrade another target molecule. Thus, the *targeting moiety* is the *carbohydrate* attached to the *enzyme*, and not the *carbohydrate* by itself (see the Specification at, *e.g.*, page 8, lines 5-9).

While Applicants thank the Examiner for suggesting languge to address the alleged defect in the claim, such language would change the meaning of the claim, and

cannot be adopted. For at least these reasons, Applicants submit that the claim accurately defines the composition and the rejection should be withdrawn.

Claims 3-5 and 7-9 were rejected under 35 U.S.C. §112, second paragraph, as allegedly beiing indefinite with respect to whether cysteine is the substituted or substituting amino acid residue. The rejection is traversed.

Claims 3, 4, and 5, from which the other rejected claims depend, clearly refer to a "cysteine that is substituted for a native amino acid other than cysteine." The Examiner's assertion that claim language encompasses the substitution of cysteine with a native amino acid that is not cysteine makes no sense in view of the plain claim language. Such an interpretation confuses the language "substituted for" with the language "substituted with," and further ignores the language "wherein said targeting moiety is joined to said enzyme through the sulfur group on a cysteine" in claim 2, and the reference to "said cysteine" in dependend claims 3 and 4. In short, the Examiner's interpretation of the claim language is not supported by the plain language of the claims.

Applicants request withdrawal of the rejection.

Claim 4 was rejected under 35 U.S.C. §112, second paragraph, as allegedly being indefinite with respect to language relating to the substrate binding site. In particular, the Examiner appears to allege that that the claim must recite an N or C-terminus for substrate binding site and that the term van der Waals contact is unclear. The rejection is traversed.

The skilled person can readily determine the location of the substrate binding site in an enzyme selected for use as part of the catalytic antagonist. Identifying the substrate binding site in a particular enzyme is not a critical element of the claim and it should not be necessary to specify the N or C-terminus as suggested by the Examiner. Applicants further traverse the rejection with respect to the "adjacent" and "van der Waals contact" language. The meaning of these terms is plain from the claim language and Applications submit that a skilled person would have no difficulty understanding such claim laguage.

Although indirectly related to the rejection, Applicants have amended claim 4 to specify that the substrate binding site binds to the target molecule (see the rejection of claim 5, immediately below).

Applicants request withdrawal of the rejection.

Claim 5 was rejected under 35 U.S.C. §112, second paragraph, as allegedly being indefinite with respect to the language "an amino acid forming a substrate binding site."

Claim 4, from which claim 5 depends, has been amended to specify that the substrate binding site binds to the target molecule.

Applicants request withdrawal of the rejection.

Claim 9 was rejected under 35 U.S.C. §112, second paragraph, as failing to recite a reference sequence.

Claim 9 has been canceled to address the rejection.

IV. Claim Rejections under 35 U.S.C. §102 and 103

Claims 1-5, 7-9, 19-23, 25, 26, 32-34, and 36 were rejected under 35 U.S.C. § 102, as allegedly anticipated by Davis *et al.* (1998) *J. Org. Chem.* 63:9614-15, and under 35 U.S.C. § 103, as allegedly obvious over Davis *et al.* in view of Nilsson *et al.* (1997) *Glycoconjugate J.* 4:219-23. These rejections are addressed together, and both rejections are traversed.

A. The Present Claims

The present claims, as exemplified by claim 1, are drawn to a catalytic antagonist of a target molecule, said antagonist comprising a targeting moiety that specifically binds to said target molecule, said targeting moiety being a carbohydrate attached to an enzyme, said enzyme being a subtilisin-type serine protease that degrades said target molecule to reduce binding of the target molecule to its cognate ligand and to said targeting moiety thereby resulting in the release of said antagonist thereby allowing said antagonist to bind and degrade another target molecule.

B. The Cited References

Davis *et al.* describe the site-selective glycosylation of a protein, which protein happens to be subtilisin from *Bacillus lentus* (paragraph bridging columns 1 and 2 on page 9614). The reference is silent as to a catalytic antagonist or the mechanism underlying such a molecule.

Nilsson *et al.* teach the synthesis of a dimeric Lewis-x hexasaccharide as a *p*-trifluoroacetamidophenylethyl-β-glycoside.

C. Analysis

The present claims relate to a catalytic antagonist of a target molecule, comprising a carbohydrate targeting moiety that specifically binds to the target molecule attached to a subtilisin-type serine protease, wherein the protease degrades the target molecule to reduce its binding to targeting moiety, resulting in the release of the antagonist, allowing it to bind and degrade another target molecule. In contrast, the teachings of Davis *et al.* are limited to the site-specific glycosylation of a polypeptide.

Nowhere do Davis *et al.* teach that that site-specific glycosylation of a polypeptides can be used to target the polypeptide to a preselected target molecule, that the subtilisin component of the glycosylated polypeptides can be used to degrade a target molecule, or that a glycosylated subtilisin can function in a catalytic manner, allowing it to degrade more than one target molecule. All these features are expressly required by the present claims, and none of the features are described by Davis *et al.* Accordingly, Davis *et al.* do not anticipate the claimed invention. Nilsson *et al.* provide no additional teaching that can be combined with Davis *et al.* to support the obviousness rejection.

In rejecting the present claims over the sited references, the Examiner appears to rely on an inherency argument to supply all the missing claims elements. However, it is well-settled patent law that inherent anticipation requires that the alleged inherent feature necessarily be present in a prior art reference – inherency cannot be established by mere probability. *Continental Can*, 948 F.2d 1264, 20 U.S.P.Q.2d (BNA) 1746 (Fed. Cir. 1991). Here, Davis *et al.* do not teach a particular carbohydrate moiety for binding to a target molecule, that the glycosylated polypeptide would bind to a target molecule, that the glycosylated polypeptide would degrade a target molecule, or that the glycosylated polypeptides would be regenerated and made available to degrade an additional target molecule. None of these features necessarily follow from what is described in Davis *et al.*; therefore, the reference does not inherently anticipate the present claims. It is especially evident that in Davis *et al.* does not teach that a carbohydrate targeting moiety that specifically binds to the target molecule, and which is attached to a subtilisin-type serine protease, can function in a catalytic manner, as expressely required by claim 1.

Since Davis *et al.* neither expressly nor inherently anticipate the present claims, withdrawal of the rejection under 35 U.S.C. § 102 is respectfully requested. Since Nilsson *et al.* provide no additional teaching that can be combined with Davis *et al.* to

support the obviousness rejection, withdrawal of the rejection under 35 U.S.C. § 103 is respectfully requested.

As discussed above and in previous Responses, Applicants submit that the Examiner has made numerous assertions about features that are allegedly inherent in the prior art, yet no objective evidence has been provided to show that such features were necessarily present. Accordingly, *should the Examiner maintain a prior art-based rejection over the sited reference in a future Office Action or Advisory Action, Applicants must insist that the Examiner file a Declaration or Affidavit clarifying the basis for the inherency argument and specifying the basis upon which the inherency argument is based.* It is not sufficient for the Examiner to merely allege inherency without meeting the legal standard as set forth in cases such as *Continental Can.*

CONCLUSION

In view of the foregoing amendments and remarks, Applicants believe the present application is fully in condition for allowance. Issuance of a formal Notice of Allowance at an early date is respectfully requested. If a telephone conference would expedite prosecution of this application, the Examiner is invited to telephone the undersigned at (650) 846-7595.

The Commissioner is authorized to charge any fees that may be required in connection with this submission and to credit any overpayments to Deposit Account No. 07-1048.

Respectfully submitted,

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/Stephen Todd/
Stephen Todd
Registration No. 47,139

Customer No. 05100
Danisco US Inc.
925 Page Mill Road
Palo Alto, CA 94304
Tel: 650-846-7595
Fax: 650-845-6504